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GUARDANT HEALTH, INC.

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

GUARDANT HEALTH, INC., a Delaware corporation, Plaintiff, vs. NATERA, INC., a Delaware corporation, Defendant.	Case No. 3:21-cv-04062 **ORIGINAL COMPLAINT** **JURY TRIAL DEMANDED**

Plaintiff Guardant Health, Inc. ("Guardant" or "Plaintiff") files this Original Complaint against Defendant Natera, Inc. ("Natera" or "Defendant") and in support thereof, alleges as follows:

I. INTRODUCTION

1. This case concerns Plaintiff's Guardant Reveal™ ("Reveal") liquid biopsy cancer assay for early-stage colorectal cancer (CRC) patients, and Defendant Natera's campaign of false and misleading advertising directed at this important and innovative diagnostic product. As the world's leading provider of comprehensive circulating tumor DNA (ctDNA) assays for clinical use, Guardant's oncology platform—including its gold-standard Guardant360®, Guardant360® CDx, and GuardantOMNI® assays—have helped improve clinical outcomes, while lowering healthcare costs, for advanced stage cancer patients around the world.

2. Leveraging its patented technology, vast data sets, and advanced analytics, Guardant recently launched Reveal, a plasma-only liquid biopsy test that detects residual and recurrent CRC in about 7 days from a simple blood draw. For oncologists, Reveal improves the management of early-stage CRC patients by detecting ctDNA in plasma after surgery, enabling doctors to identify patients with residual CRC who may benefit from post-surgery chemotherapy (adjuvant chemotherapy), months earlier than current standard-of-care tests permit. Reveal is the first test for minimal residual disease (MRD) detection that detects ctDNA in the plasma of CRC patients following treatment ***without the need for a tissue sample and sequencing*** to determine the particular mutations that were present in the patient's tumor. Reveal achieves outstanding sensitivity (91%) for predicting recurrence of CRC disease.

3. With little or no concern for the CRC patients who could be harmed, Natera has undertaken a campaign of misinformation to convince customers and potential customers, including oncologists and other physicians, cancer researchers, health care institutions, biopharmaceutical companies, and genetic laboratories, to avoid using Reveal in favor of Natera's own Signatera™ ("Signatera"), a tumor-dependent assay. In its commercial advertising and promotion, Natera makes literally false and misleading statements that disparage Guardant's new assay, and falsely asserts that Signatera is superior to Reveal across a variety of metrics, including sensitivity,[1] failure rate,[2] negative predictive value (NPV),[3] and Hazard Ratio,[4] among other categories. These claims are false. Natera combines outright misrepresentations with scientifically unfounded comparisons based on cherry-picked metrics, data artifacts, and

[1] "Sensitivity" refers to the assay's ability to identify which patients will develop recurrences based on MRD detection by ctDNA assay. A higher percentage indicates a test is more sensitive.

[2] "Failure rate" refers to the percentage of time a ctDNA assay fails to provide a result at all, whether positive or negative. For any test, a lower failure rate is more desirable.

[3] "NPV" refers to the assay's ability to correctly predict which patients will subsequently not develop a recurrence of CRC (i.e., a "negative" test result means CRC will not recur).

[4] The "Hazard Ratio" refers to a comparison between the recurrence rate over time in CRC patients who tested positive for MRD by ctDNA assay, to the recurrence rate in CRC patients who tested negative for MRD by ctDNA. A larger hazard ratio suggests that the assay is potentially more useful in successfully distinguishing CRC patients whose cancers will or will not recur.

noncomparable clinical studies to exaggerate the purported benefits of Signatera while inaccurately denigrating Reveal. In truth, Reveal has important clinical advantages over Signatera—including its superior landmark sensitivity, its availability for patients from whom tumor samples are unavailable, and its faster initial turnaround time from sample collection to assay results—all of which Natera ignores.

4. Guardant seeks to enjoin Natera from continuing to make or disseminate false and misleading statements about the performance of Reveal and Signatera; to require Natera to retract, remove, and correct these false and misleading advertising claims; and to recover damages and other relief for the harm that Natera has inflicted on Guardant.

II. PARTIES

5. Plaintiff Guardant is a Delaware corporation having its principal place of business at 505 Penobscot Dr., Redwood City, California 94063.

6. Guardant was founded in 2012 by pioneers in DNA sequencing and cancer diagnostics. Since its inception, Guardant has focused its expertise on the development of liquid biopsy assays for cancer. It was the first company to develop and commercialize a comprehensive liquid biopsy assay to identify genomic biomarkers for advanced solid tumors using cell-free ctDNA, from simple, non-invasive blood draws.

7. Today, Guardant is a leading precision oncology company focused on helping conquer cancer globally through the use of its proprietary blood tests, vast data sets, and advanced analytics. The Guardant oncology platform leverages its capabilities to drive commercial adoption, improve patient clinical outcomes, and lower healthcare costs across all stages of the cancer care continuum. Guardant Health has commercially launched the liquid biopsy-based Guardant360®, Guardant360® CDx, and GuardantOMNI® tests for advanced stage cancer patients, and recently launched its Reveal test for early-stage CRC patients.

8. Defendant Natera is a Delaware corporation having its principal place of business at 13011 McCallen Pass, Building A, Suite 100 Austin, Texas 78753, and offices at 201 Industrial Rd., San Carlos, California 94070. Natera may be served with process by serving a copy of this Complaint on its Registered Agent: National Registered Agents, Inc., 1209 Orange

Street, Wilmington, Delaware 19801.

9. Natera markets and sells Signatera, a product it describes as a "personalized, tumor-informed assay optimized to detect circulating tumor DNA (ctDNA) for molecular residual disease (MRD) assessment and recurrence monitoring for patients previously diagnosed with cancer." Signatera competes with Reveal in the market for ctDNA assays that can be used after surgery on CRC patients, to detect recurrences and evaluate the need for adjuvant chemotherapy.

III. JURISDICTION AND VENUE

10. This is an action for false advertising under Section 43(a) of the Lanham Act, 15 U.S.C. § 1125(a); for false advertising in violation of Cal. Bus. & Prof. Code § 17500 et seq.; for unlawful trade practices in violation of Cal. Bus. & Prof. Code § 17200 et seq.; and for unfair competition in violation of the common law of California and other states in which Defendant is conducting its activities.

11. This Court has subject matter jurisdiction over this action pursuant to 28 U.S.C. §§ 1331 and 1338 and 15 U.S.C. §§ 1051, et seq.

12. This Court has jurisdiction over Plaintiff's state law claims pursuant to 28 U.S.C. § 1367 and the doctrine of supplemental jurisdiction.

13. The exercise of personal jurisdiction in California is proper both because of Defendant's ongoing and systematic contact with California and the Northern District of California, including its maintenance of a regular place of business in the District, and because acts giving rise to Plaintiff's causes of action have occurred in the Northern District of California. Specifically, Natera markets, promotes, advertises, offers for sale, sells, and/or distributes Signatera to customers including oncologists and other physicians, cancer researchers, health care institutions, biopharmaceutical companies, genetic laboratories, and/or others throughout the United States, including in the Northern District of California. Defendant has purposefully and voluntarily placed Signatera into the stream of commerce with the expectation that this product will be purchased by customers in the Northern District of California. Furthermore, Natera falsely and misleadingly advertises Signatera to customers, including

oncologists, pathologists, additional physicians, health care institutions, pharmaceutical companies, and/or others throughout the United States, including in the Northern District of California.

14. Venue is proper in the Northern District of California pursuant to 28 U.S.C. § 1391.

IV. FACTUAL BACKGROUND

A. Early Identification of At-Risk Patients is a Key to Preventing Recurrence of Colorectal Cancer and Prolonging Survival

15. Colorectal cancer (CRC) is the third most commonly diagnosed cancer and the second leading cause of cancer death in the United States in both men and women. While a majority of patients are diagnosed with early-stage disease, nearly a third of patients whose CRC spreads into adjacent tissues and lymph nodes will die from their disease within five years.

16. Surgery alone is often curative for early-stage CRC, and in later-stage cases, adjuvant chemotherapy after surgery can reduce the risk of recurrence. However, clinicians have had very limited means of identifying patients that require adjuvant chemotherapy. Thus, the development of effective clinical tests to identify CRC patients with MRD—i.e., a small number of CRC cells remaining in the body that can later multiply and cause recurrence of the disease—after surgery has long been recognized as a need, to help doctors both identify patients who may benefit from additional therapy, and avoid administering unnecessary and toxic treatment to patients who will not benefit from it.

17. Because residual cancer cells that remain in the body following treatment typically cause no physical signs or symptoms and are present at very low levels that are undetectable with standard techniques, detecting and monitoring MRD has required development of advanced and highly sophisticated technologies with the requisite precision and sensitivity for clinical decision-making. Reveal provides that sophisticated technology.

B. Liquid Biopsy Technology Allows Assessment of MRD by Detecting Circulating Tumor DNA in Blood

18. Human blood contains fragments of DNA that are shed into the bloodstream by

dying cells in tissues—including cancers. Such fragments derived from tumor cells are known as circulating tumor DNA (ctDNA). This phenomenon led to the development of so-called "liquid biopsies" a game-changing technology capable of detecting the presence of cancer in patients by detecting ctDNA in their blood, and eventually led to liquid biopsies specifically designed to assess MRD following treatment of CRC. Liquid biopsies using simple blood draws offer major advantages for identifying MRD, because they are quick, convenient, and minimally invasive, and can be easily repeated to monitor for the presence of ctDNA over time.

19. However, detecting and characterizing the very low concentrations of ctDNA present in the blood of patients with MRD, and using that information to stratify CRC patients as high- or low-risk for recurrence, requires an assay that is both highly sensitive and specific. Recognizing this need, Guardant expended substantial resources and time to develop Reveal, a clinical blood-based assay to evaluate ctDNA in blood using advanced DNA sequencing methods. Launched in February 2021, Reveal is the first commercially available plasma-only ctDNA assay, capable of detecting MRD in post-operative CRC patients without the need for prior sampling and sequencing of tumor tissue or the time needed to create a new, customized test for each new patient.

20. Most important, Reveal ***works***: Peer-reviewed data published by Parikh et al. in the journal Clinical Cancer Research shows that Reveal offers 91% recurrence sensitivity (i.e., ability to identify which patients will recur based on ctDNA detection) and 100% positive predictive value[5] for recurrence (i.e., all patients Reveal identified as having a "positive" ctDNA test result later recurred).

21. Natera offers a liquid biopsy MRD assay it calls Signatera, which it launched commercially in 2019. Natera advertises, promotes, markets, and sells Signatera to oncologists and other physicians, cancer researchers, health care institutions, biopharmaceutical companies, genetic laboratories, and others nationwide, including in California. Unlike Reveal, Signatera is a

[5] Positive predictive value (PPV) refers to the assay's ability to correctly predict which patients will subsequently develop a recurrence of CRC (i.e., "positive" test result means CRC will recur).

"tumor-informed" (tumor-dependent) assay. It requires initial genomic profiling of tumor tissue taken from the individual patient. Information from the tumor tissue is then used to identify a panel of tumor-derived mutations specific to that patient, which then can be monitored through testing of blood samples collected throughout the patient's disease course.

22. Tumor-dependent assays like Signatera have meaningful drawbacks. Specifically, a significant number of CRC patients—particularly those treated with chemotherapy prior to surgery—may not have sufficient samples of tumor tissue to allow initial genomic profiling of the tumor. For these patients, a plasma-only ctDNA assay like Reveal provides the ***only*** option for MRD detection using ctDNA. Furthermore, acquiring sufficient tissue specimens can be painful, dangerous, time consuming and create significant delays in MRD testing turnaround time. Reveal reduces the time spent waiting for results needed to decide whether high-risk patients require adjuvant chemotherapy from approximately three weeks to 7 days. For patients with a potentially lethal disease, this reduction in wait time is critical for both outcomes (earlier initiation of chemotherapy has been associated with improved outcomes) and for peace of mind.

C. Natera's Advertising Falsely Claims that Signatera is Superior to Reveal, and that Reveal is Unproven and Insensitive

23. Fearful that Signatera cannot compete with Reveal and Guardant on the merits, Natera falsely and misleadingly advertises and promotes Signatera in comparison to Reveal. In its advertising, Natera deceptively characterizes Reveal as unproven, insensitive, and consequently and unfoundedly "detrimental to patients," while touting Signatera's supposed superiority.

24. Natera's advertising is based on irrelevant metrics, misrepresented data artifacts, and misleading and inapt comparisons, presented in disregard of the actual scientific evidence supporting Reveal's substantial benefits for oncologists and their patients. Carefully timed to coincide with the very launch of Reveal, Natera's false and misleading comparisons of Reveal and Signatera have harmed Guardant, and will continue to cause Guardant irreparable harm if not stopped.

1. Natera's Advertising Falsely Claims Signatera Is Superior to Reveal

25. Shortly after Reveal's commercial launch in February 2021, Natera began contacting both its and Guardant's current and potential customers, including leading cancer centers like the Mayo Clinic, expressing supposed "concern" about "other laboratories rushing into the clinical MRD market and making potentially misleading claims" that Natera asserted "may be detrimental to patients." In a "Dear Colleague" advertisement dated March 2, 2021, which, on information and belief, Natera widely emailed to both its and Guardant's customers and potential customers, Natera stated:

> Natera is committed to the science and precision of molecular residual disease (MRD) testing for improving patient care. We are proud that Signatera data has been published or presented from over 2,000 patients across 30+ tumor histologies. As this exciting field gains momentum, especially in early-stage CRC, there is concern about other laboratories rushing into the clinical MRD market and making potentially misleading claims with no peer-reviewed evidence, which may be detrimental to patients. As you review the evidence for any new MRD test, please keep in mind several minimum requirements for MRD product performance and clinical validation

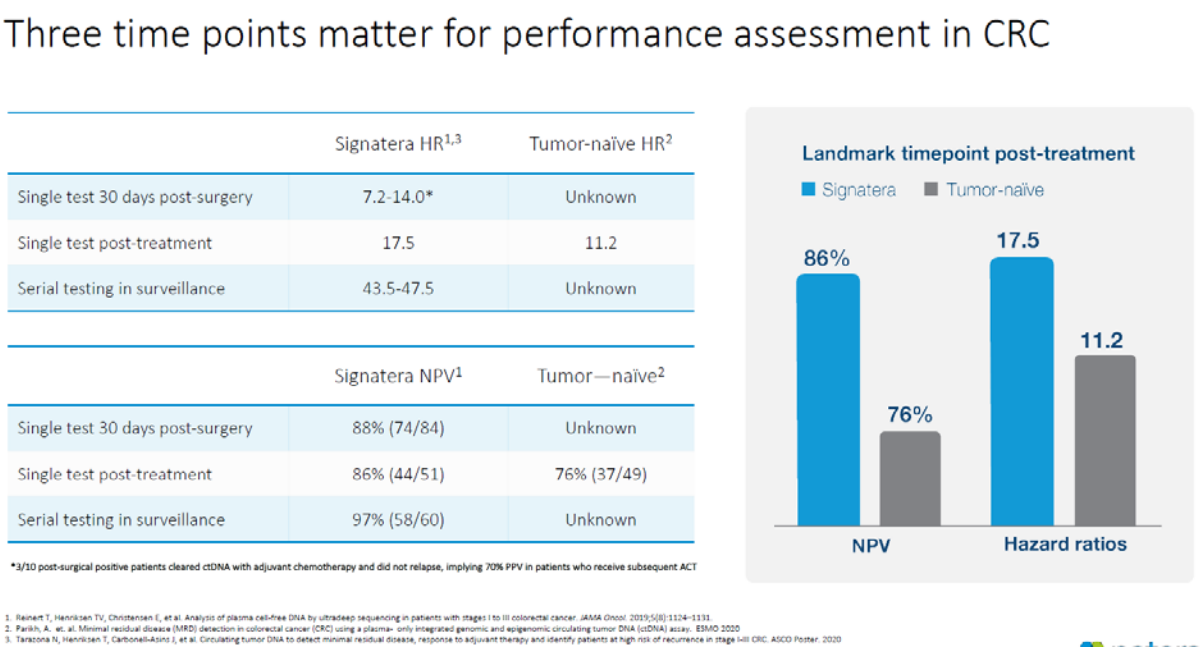
(emphasis in original).

26. In the same promotional email, Natera sent these customers and potential customers a slide presentation entitled "Evidence Review: Tumor-informed vs. tumor-naïve MRD." Though not identifying Reveal by name, Natera's presentation expressly references data presented by "Parikh, A. et al." at the 2020 European Society for Medical Oncology (ESMO) conference—a study specifically concerning Reveal. Moreover, Reveal is the ***only*** "tumor-naïve" (that is, plasma-only) ctDNA assay for detecting MRD in CRC patients available on the market, and is also the only ctDNA assay for MRD introduced at or around the time Natera sent this presentation.

27. Natera's "Evidence Review" falsely criticizes "tumor-naïve methods," that is, Reveal, as unsupported by "peer-reviewed evidence." In fact, interim data from the very study cited by Natera—Parikh et al.—was peer-reviewed before being published, first as abstract-presentations at three separate prestigious scientific meetings (ASCO 2019, ESMO 2019, and ESMO 2020), and later as an article in the April 29, 2021 issue of the journal Clinical Cancer

Research.

28. Natera further erroneously claims that, while Signatera's "test performance" is "unsurpassed," Reveal is not only inferior to Signatera, but has "unknown" performance with respect to sensitivity and hazard ratios for two of three "time points" that "matter":



Three time points matter for performance assessment in CRC

	Signatera HR[1,3]	Tumor-naïve HR[2]
Single test 30 days post-surgery	7.2-14.0*	Unknown
Single test post-treatment	17.5	11.2
Serial testing in surveillance	43.5-47.5	Unknown

	Signatera NPV[1]	Tumor—naïve[2]
Single test 30 days post-surgery	88% (74/84)	Unknown
Single test post-treatment	86% (44/51)	76% (37/49)
Serial testing in surveillance	97% (58/60)	Unknown

*3/10 post-surgical positive patients cleared ctDNA with adjuvant chemotherapy and did not relapse, implying 70% PPV in patients who receive subsequent ACT

1. Reinert T, Henriksen TV, Christensen E, et al. Analysis of plasma cell-free DNA by ultradeep sequencing in patients with stages I to III colorectal cancer. JAMA Oncol. 2019;5(8):1124–1131.
2. Parikh, A. et. al. Minimal residual disease (MRD) detection in colorectal cancer (CRC) using a plasma- only integrated genomic and epigenomic circulating tumor DNA (ctDNA) assay. ESMO 2020
3. Tarazona N, Henriksen T, Carbonell-Asins J, et al. Circulating tumor DNA to detect minimal residual disease, response to adjuvant therapy and identify patients at high risk of recurrence in stage I-III CRC. ASCO Poster. 2020

29. These statements too are false, as explained below. But rather than correcting its falsehoods, Natera repeated and amplified them—repeatedly.

30. Shortly after Natera distributed its "Evidence Review," Parikh et al.'s previously presented data supporting the clinical performance of Reveal, derived from plasma specimens from 84 CRC patients undergoing curative intent surgery, was published in the peer-reviewed journal Clinical Cancer Research. Nonetheless, Natera renewed and repeated its previous criticisms of Reveal on its website, including in a broadly misleading "white paper to learn how our tumor-informed approach stacks up against a tumor naïve assay" found at https://www.natera.com/wp-content/uploads/2021/05/SGN_WP_Solar_20210503_NAT-9000052_FINAL_DWNLD.pdf.

31. In its white paper, which Natera publishes on its website to influence customers and potential customers to purchase Signatera rather than Reveal, Natera purports to compare "Signatera (tumor informed assay)" to a "Tumor-naïve assay," that is, plasma-only Reveal, citing

data that appear to show—again, falsely—that Reveal is "not validated," or that Signatera significantly outperforms Reveal on every referenced metric, including "Hazard ratios" and "Negative predictive value (NPV)":

Table 3. *Comparison of hazard ratios and negative predictive values of tumor-informed and tumor-naive assays in early-stage CRC*

	Signatera (tumor-informed assay)[4,7,8]	Tumor-naive assay[19]
Hazard ratios of ctDNA (positive vs negative)		
Post-surgery (30 day single test)	7.2-14.0*	Not Validated
Post-ACT (single test)	17.5	9.8-11.2**
Serial testing	43.5-47.5	11.4
Negative predictive value (NPV)		
Post-surgery (30 day single test)	88% (74/84)	Not Validated
Post-ACT (single test)	86% (44/51)	76% (37/49)**
Serial testing	97% (58/60)	82% (41/50)

32. Natera's white paper further asserts that: "Without the genomic information for each primary tumor, tumor naïve assays are unable to filter out background biological noise from CHIP or to avoid tracking driver mutations that may be subjected to selection pressure from treatment . . . ."[6] But this is false; Reveal can and does filter out CHIP background noise bioinformatically. In fact, data publicly presented in 2018 on a prototype of the Reveal assay showed 100% specificity with incorporation of the CHIP filter.

33. In May 2021, Natera also published on its public-facing website advertising entitled "Investor presentation," which purports to compare "Signatera vs. Reveal performance":

[6] "CHIP" refers to clonal hematopoiesis of indeterminate potential—mutations from blood cells that can lead to false positive results when testing for MRD.

Signatera vs. Reveal performance comparison

	Signatera	Reveal
Validation data published or presented (# patients analyzed)	> 2,000[1,2]	< 150[4,5]
Pre-surgical sensitivity in CRC	89-94%[1,3]	47%*[4]
Failure rate in CRC – tissue and plasma combined	< 3%[3]	12-14%[4]
Number of blood tubes required	2	4
Diagnostic lead time vs. radiographic recurrence in CRC (avg)	8.7 months[1]	~4 months*[4]
Post-surgical NPV/PPV in CRC (30 days post-surgery)	88% / 100%**[1]	not reported[4]
Serial longitudinal NPV in CRC	97%[1]	82%[4]
Serial longitudinal Hazard Ratio in CRC	43.5[1]	11.4[4]
Serial longitudinal sensitivity in CRC	88-94%[1,2]	69%[4]
Quantitation of ctDNA burden for monitoring purposes	Tumor copies per mL	none

34. Shortly after posting the May 2021 performance comparison on its website, Natera began disseminating it—repeatedly—to the same customers and potential customers in order to tout Signatera's supposed superiority over Reveal.

35. Similar to its "Evidence Review" and white paper advertising, Natera's May 2021 performance comparison claims to demonstrate quantitatively that Signatera is superior to Reveal across a wide-ranging set of metrics. Here, these metrics purportedly include "pre-surgical sensitivity," "failure rate," "diagnostic lead time," [7] "post-surgical" and "serial longitudinal" negative predictive value (NPV), and "Hazard Ratio," among other categories. All of this is false and misleading.

2. Natera's Advertising is False and Misleading

36. In reality, each of Natera's promotional claims of superiority, including the express and implied claims contained in its "Evidence Review," white paper, and the "Signatera vs. Reveal performance comparison" are false and misleading. They also either deceived or are likely to deceive oncologists and other physicians, cancer researchers, health care institutions, biopharmaceutical companies, and genetic laboratories, and other customers and potential

[7] "Diagnostic lead time" refers to the time between the first MRD detection by ctDNA assay and the first confirmation of CRC recurrence by standard radiographic imaging methods. A longer diagnostic lead time is generally observed with higher sensitivity tests.

customers into believing that Reveal is untested, inaccurate, insensitive, and inferior to Signatera.

37. Any valid comparison between diagnostic tests, including ctDNA assays for detecting MRD in CRC patients—and specifically including Signatera and Reveal—must be supported by properly designed, head-to-head studies that directly compare the two assays using the same test procedures and protocols in the same patient population. Cross-test comparisons, especially where the purpose and methodology of the underlying studies differ significantly, and/or where the studies are conducted in different patient populations, necessarily lead to a misleading apples-to-oranges result that cannot legitimately be used to claim that one test is superior to the other.

38. To date, no such head-to-head studies involving Signatera and Reveal and using the same test protocol and study population are available. Instead, Natera's purported comparisons of the "performance" of Signatera vs. Reveal largely rely on data published by Parikh et al. concerning Reveal, and data published by Reinert et al. for Signatera. These different studies used very different test protocols and analysis methods, and examined very different patient populations. Consequently, Natera's claims of superiority based on these improper comparisons are false, misleading, and deceptive.

39. In fact, many of Natera's cherry-picked comparison metrics are unrelated to assay "performance" at all. While Natera touts the number of "patients analyzed" in "published or presented studies," which Natera claims is more than two thousand for Signatera, those numbers do not prove the superiority of the clinical *performance* of one ctDNA assay over another. Moreover, the ">2,000" number reported for Signatera is inflated. It double-counts some patients whose data were used in more than one published study, and it includes patient populations presenting with cancers other than CRC for which Reveal is neither validated nor intended to be used.

40. Likewise, Natera claims that Signatera requires only two "blood tubes," while Reveal requires four. But again, this is not a "performance" metric at all. But even there, Natera's representation that Reveal "requires" 4 tubes is false. Reveal, like Signatera, only requires 2 tubes of blood. Unlike Natera, Guardant's Reveal kit collects 2 additional tubes of

blood to provide redundancy in the rare event of an assay failure on the first 2 blood tubes; thereby protecting patients from having to provide another blood sample and saving valuable time.

41. Finally, "quantitation of ctDNA for monitoring purposes" is an assay *feature*, not an appropriate measure of assay *performance*. Natera's assertions that quantitation, i.e., "quantitative results," is necessary to achieve good assay performance, or is an "MRD assay requirement," are misleading. This is particularly so in light of the intended use of both the Signatera and Reveal assays: to identify CRC patients at increased risk for recurrence of the disease. All available evidence shows that the presence of ctDNA—regardless of the quantity—indicates a high likelihood of recurrence. As such, the clinical utility of ctDNA quantitation in the context of the intended use of the assay is unclear, at best. Natera's assertion that "quantitation is essential for monitoring tumor response during the patient's treatment," is unsupported by any studies showing that an improvement in patient outcome is achieved by knowing or acting on changes in ctDNA quantity during treatment. Because it is wholly unsupported, Natera's claim is false. Signatera's practice of reporting a "mean tumor molecules per mL" value, and Reveal's choice not to do so, does not represent a performance advantage for one over the other.

42. While these false and misleading claims are harmful, it is Natera's misrepresentations concerning Reveal's actual performance metrics that are the most damaging to Guardant and its new assay.

43. **Failure rate:** Natera's comparison of "failure rate in CRC," and its claim of Signatera's superiority over Reveal, are false. As the article published by Parikh et al. in the April 29, 2021 issue of Clinical Cancer Research states, this study—which Natera cites as proof that Reveal has a "12-14%" failure rate (vs. a "< 3%" rate for Signatera)—relied on ***banked*** plasma or cell free DNA samples that had input amounts substantially less than recommended. Indeed, as Parikh et al. stated explicitly in the cited publication, "the extracted ctDNA quantity or quality was below the recommended and optimal input levels for the assay" and "may have affected overall performance characteristics." In point of fact, the actual failure rate of Reveal in

patient care testing is ***less than 1%***, better than Signatera's claimed failure rate of less than 3%.

44. **Pre-surgical sensitivity:** Natera's claims of Signatera's superior "pre-surgical sensitivity" ("89-94%" vs. "47%") is functionally meaningless and highly misleading. Reveal is not intended or indicated to be used as a diagnostic tool pre-surgery. And, as an assay that relies on the existence of surgically-excised tumor tissue, Signatera ***cannot*** be used as a pre-surgical diagnostic tool (meaning it has a real-world pre-surgical clinical sensitivity of 0%). Moreover, the study Natera cites as the source of this statistic—Parikh et al.—contains a population where nearly half (45%) of the study cohort had received chemotherapy prior to surgery and in which the pre-surgical sample volumes were far lower than recommended. Such pre-surgical treatment suppresses ctDNA, and thus necessarily lowers the ctDNA detection rate and low sample volume also can affect assay sensitivity.

45. **Post-surgical NPV/PPV:** Natera's further comparison of the 30-day post-surgical negative and positive predictive value (NPV/PPV) for Signatera vs. Reveal, (i.e., 88%/100% vs. "not reported" or "not validated"), is similarly misleading. For many CRC patients, surgery to remove the tumor does not represent the end of the patient's initial treatment regimen; many patients receive adjuvant chemotherapy. While—contrary to Natera's claim—Parikh et al. ***did*** report data that could be used to calculate a 30-day post-surgical NPV and PPV for Reveal, they ***did not*** focus on—nor did they draw conclusions from—data from this timepoint. The 30-day post-surgical MRD timepoint is relevant for clinical MRD testing to assist with adjuvant therapy decisions during patient care. It is not the appropriate timepoint in an observational/retrospective research study to validate certain performance metrics, like PPV or NPV, of assays like Signatera or Reveal that are intended to predict disease recurrence.

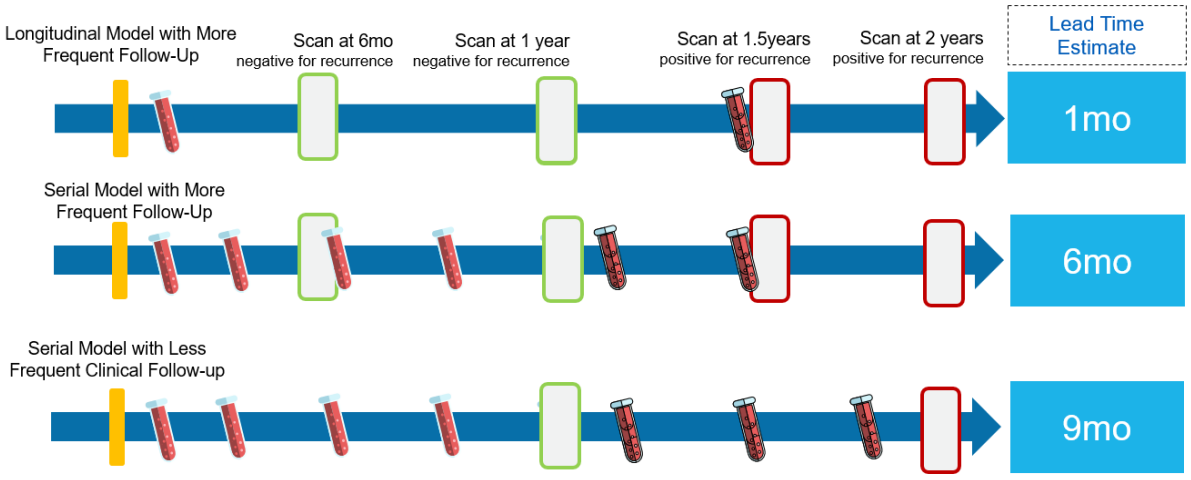
46. Simply put, adjuvant therapy works, and can cure MRD-positive patients that otherwise would have recurred. As such, estimates of an assay's NPV and PPV, when sourced from samples collected after surgery but before adjuvant chemotherapy, are confounded by the effect of chemotherapy and are uninterpretable—one cannot sort out the merits of the assay from the effects of the chemotherapy. Parikh et al. purposely chose to report data from samples collected after all definitive treatment to avoid this confounding factor precisely because nearly

55% of the study participants received additional treatment post-surgery.

47. Meanwhile, other assay performance metrics, such as sensitivity to detect recurrence are not subject to the confounding effect of post-operative chemotherapy. Nor is sensitivity to detect recurrence subject to the confounding effects of the baseline population risk, as described below. Thus sensitivity would be a more appropriate metric to compare assay performance at the 30-day post-surgery timepoint than NPV. However, Natera chose not to report this metric in its marketing materials, presumably because it shows Signatera's performance is *less* favorable compared to Reveal. As reported by Reinert et al., the sensitivity of Signatera to detect recurrence using the 30-day post-surgical timepoint is 7/17 patients (41%). This metric as reported by Parikh et al. in the supplemental data shows 14/26 patients (54%). Among the subset of patients with stage I-III disease (excluding stage IV patients, a more similar stage representation to the Reinert et al. data), the Reveal data still show an even higher sensitivity for recurrence of 9/16 (56%).

48. In short, PPV as a metric of assay validity must be taken from samples collected after all therapy is complete and where sufficient follow-up is available. Underscoring the importance of this—and the misleading nature of the values presented by Natera's advertising—the PPV for both assays is **100%** when these conditions are met.

49. **Diagnostic lead time:** Natera's unfavorable comparison of Reveal's "diagnostic lead time vs. radiographic recurrence," to that of Signatera, is also false and misleading. The calculation of a "diagnostic lead time estimate" is affected as much by the frequency of the tests that are used to derive the estimate as it is by the assay's sensitivity. As the following graphic shows, the diagnostic lead time estimate for the ***same assay and the same patient with same test results*** can vary significantly, depending on how often follow-up testing is conducted.



50. Because Natera's diagnostic lead time estimates are derived from studies having different protocols and testing regimens, its comparison is fundamentally flawed and unreliable. The "diagnostic lead time estimate" for Signatera was developed from data reported by Reinert et al. Reinert's study protocol called for CRC patients to undergo ctDNA testing 30 days after surgery, and every three months afterwards, for three years or until the patient's death or withdrawal from the study. In contrast, the study by Parikh et al. did not involve patient testing at regular intervals over a specified period of time and was not designed to estimate "diagnostic lead time." Consequently, Parikh et al. did not report an estimated diagnostic lead time for Reveal, and the "~ 4 months" value Natera fabricated for Reveal has no reliable basis in fact.

51. **"Serial longitudinal" NPV, hazard ratio, and sensitivity:** Likewise, Natera's comparisons of the "serial longitudinal" NPV, hazard ratio, and sensitivity of Signatera and Reveal are fundamentally misleading. Parikh et al.'s study of Reveal was not designed to provide "serial" test data (i.e. testing at regular time intervals after the initial test), and consequently did not report these statistics. Natera nevertheless biased its comparison with Reveal in Signatera's favor by reporting Parikh et al.'s "***longitudinal***" sensitivity of 69%, which is calculated in patients who had at least one surveillance draw, the timing of which was highly variable relative to the time of recurrence, and is in no way similar to the timing of sample collection employed by Reinert et al. This is fundamentally a misleading apples-to-oranges comparison. However, the Parikh et al. study includes a subset of recurrence positive patients who had a Reveal sample available within 4 months of recurrence. Using these data to estimate the "***serial*** longitudinal"

sensitivity parameter, Reveal has an estimated sensitivity of 91%–comparable (or superior) to Signatera. Despite the valid estimate of 91% being clearly outlined in the Parikh et al. paper, Natera chose to use a fabricated and invalid "longitudinal" sensitivity estimate, again presumably because it cast Reveal in a less favorable light.

52. Beyond its choice to disregard differences in testing frequency, Natera further biased its serial longitudinal NPV and hazard ratio comparisons by ignoring the significant differences in the patient populations from which the data were drawn. The Reinert et al. study using Signatera examined patients with stages I to III CRC, where the CRC recurrence rate was 19% (24/125 evaluable patients). In contrast, the patients included in the Parikh et al. study were more than twice as likely to recur (39%, 27/70 evaluable patients) demonstrating that the patients in this study had a much higher risk of disease recurrence than those studied by Reinert et al. Assays of equal sensitivity and specificity yield dramatically different NPVs and hazard ratios when applied to patient populations with different risk profiles. Natera's deliberate failure to account for this difference results in false and highly deceptive comparisons.

D. Natera's False and Misleading Advertising Has Caused or Will Likely Cause Harm to Patients and to Guardant

53. Natera's commercial advertising and promotions have had their intended effect. Natera's efforts to disparage the performance of Reveal while falsely touting Signatera has misled or is likely to mislead oncologists, healthcare institutions, and other potential customers, and caused these customers to order Signatera rather than Reveal for their CRC patients.

54. In addition, Natera's false statements regarding Reveal have injured, or are likely to injure, the reputation of this product and the reputation of Guardant itself, costing Guardant customer good will and causing the loss of future sales. Natera's express and necessarily implied assertions that Reveal has "significant gaps in study design and performance," and is less sensitive and predictive than Signatera, sow doubt among oncologists and others about the utility and performance of Reveal. Natera explicitly reinforces this doubt by warning doctors that using Reveal may "be detrimental to patients." Natera's assertions will cause, and on information and belief may have already caused, some CRC patients to lose opportunities for rapid MRD

detection and the attendant benefits of timely guided treatment decisions. They are also likely to cause irreparable harm to Guardant's business and reputation.

55. By misleading oncologists and other medical professionals into believing that Reveal is unsupported, insensitive and inferior to Signatera, Natera has caused patients to miss the benefits of Guardant's validated and effective plasma only liquid biopsy assay.

COUNT I:
FALSE ADVERTISING IN VIOLATION OF SECTION 43(a)(1)(B) OF THE LANHAM ACT, 15 U.S.C. § 1125(a)(1)(B)

56. Plaintiff repeats and hereby realleges the allegations above as if fully set forth herein.

57. In its commercial advertising and promotion to potential customers, Defendant markets Signatera by stating and implying that Reveal suffers from significant gaps in study design and performance, and that Signatera's performance is superior to Reveal.

58. Defendant's promotional claims about the relative clinical support and performance of Reveal and Signatera are false and/or misleading. The data Defendant relies upon to draw its comparisons in favor of Signatera are derived from studies conducted by different researchers, employing different methodologies and procedures, using different patient populations, and having different qualities and characteristics that do not permit a fair or valid comparison. Defendant disregards data that show Reveal has excellent clinical performance.

59. These claims violate Section 43(a) of the Lanham Act, which provides in relevant part that a "person who, or in connection with any goods or services . . . uses in commerce any . . . false or misleading description of fact or misleading representation of fact, which . . . in commercial advertising or promotion, misrepresents the nature, characteristics, qualities, or geographic origin of his or her or another person's goods, services, or commercial activities, shall be liable to a civil action by any person who believes that he or she is likely to be damaged by such act."

60. Defendant's promotional claims about the performance of Reveal, alone and in comparison to Signatera, are material. The clinical characteristics and performance of cancer diagnostic procedures are of paramount importance to doctors responsible for treating patients

with life-threatening illnesses like CRC.

61. Pursuant to 15 U.S.C. § 1117, Plaintiff is entitled to damages for Defendant's Lanham Act violations, an accounting of profits made by Defendant on sales of its product, as well as recovery of the costs of this action.

62. Defendant's acts are willful, wanton and calculated to deceive, and are undertaken in bad faith, making this an exceptional case entitling Plaintiff to recover reasonable attorneys' fees pursuant to 15 U.S.C. § 1117.

63. Unless enjoined by this Court, Defendant's acts will irreparably injure Plaintiff's goodwill and erode its market share. Pursuant to 15 U.S.C. § 1116, Plaintiff is entitled to preliminary and permanent injunctive relief to prevent Defendant's continuing acts..

COUNT II:
FALSE ADVERTISING IN VIOLATION OF CAL. BUS. & PROF. CODE § 17500 ET SEQ.

64. Plaintiff repeats and hereby realleges the allegations above as if fully set forth herein.

65. Plaintiff brings this cause of action pursuant to CAL BUS. & PROF. CODE § 17535 in an individual capacity and not on behalf of the general public.

66. CAL. BUS. & PROF. CODE § 17500 provides that it is unlawful for any person, firm, corporation, or association to dispose of property or perform services, or to induce the public to enter into any obligation relating thereto, through the use of untrue or misleading statements.

67. CAL. BUS. & PROF. CODE § 17508 provides:

> It shall be unlawful for any person doing business in California and advertising to consumers in California to make any false or misleading advertising claim, including claims that (1) purport to be based on factual, objective, or clinical evidence, that (2) compare the product's effectiveness or safety to that of other brands or products, or that (3) purport to be based on any fact.

68. Defendant's misleading statements violate CAL. BUS. & PROF. CODE §§ 17500 and 17508, and Plaintiff has acted in response to and reliance on the misleading statements made by Defendant regarding the performance of Signatera and Reveal, including by expending time,

money, and other resources on preparing its sales force to respond to these misleading statements.

69. Defendant's conduct has caused Plaintiff damage in an amount to be determined at the trial herein but not less than $75,000 and, unless enjoined by this Court, Defendant's conduct will continue to cause Plaintiff irreparable damage for which Plaintiff has no adequate remedy at law.

70. Pursuant to CAL. BUS. & PROF. CODE § 17535, Plaintiff seeks an order of this Court compelling the Defendant to provide restitution, and to disgorge the monies to which Plaintiff is entitled but were instead collected and realized by Defendant as a result of its false and misleading statements and injunctive relief enjoining Defendant from making such false and misleading statements.

COUNT III:
UNLAWFUL TRADE PRACTICE IN VIOLATION OF CAL. BUS. & PROF. CODE § 17200 *ET SEQ.*

71. Plaintiff repeats and hereby realleges the allegations above as if fully set forth herein.

72. Pursuant to CAL. BUS. & PROF. CODE § 17200, unfair competition is "any unlawful, unfair or fraudulent business act or practice and unfair, deceptive, untrue or misleading advertising . . . ." The misleading statements made by Defendant regarding the performance of Signatera in comparison to Plaintiff's Reveal violate CAL. BUS. & PROF. CODE § 17200 et. seq. Moreover, Defendant's conduct constitutes a violation of the Lanham Act, and thus as unlawful business conduct is separately actionable as a violation of CAL. BUS. & PROF. CODE § 17200 et. seq. Defendant's conduct is also otherwise unfair and therefore a violation of these provisions.

73. Defendant's conduct has caused Plaintiff damage in an amount to be determined at the trial herein, and, unless enjoined by this Court, Defendant's conduct will continue to cause Plaintiff irreparable damage for which Plaintiff has no adequate remedy at law.

74. Pursuant to CAL. BUS. & PROF. CODE § 17203, Plaintiff seeks an order of this Court compelling the Defendant to provide restitution, and to disgorge the monies to which Plaintiff is entitled but were instead collected and realized by Defendant as a result of its false

and misleading statements and injunctive relief enjoining Defendant from making such false and misleading statements.

COUNT IV:
COMMON LAW UNFAIR COMPETITION

75. Plaintiff repeats and hereby realleges the allegations above as if fully set forth herein.

76. With full knowledge of Plaintiff's Reveal, Defendant has made false and misleading explicit and implicit representations to potential customers, and others that Defendant's Signatera offers superior performance compared to Reveal.

77. Defendant's false and misleading statements and omission of relevant facts are likely to cause and have caused confusion, mistake, or deception about the nature, characteristics and qualities of Defendant's Signatera in comparison, connection, or association with Plaintiff's Reveal.

78. Defendant knows, or in the exercise of reasonable discretion should know, that its marketing program deceives potential customers about the nature, characteristics, and qualities of Signatera in comparison, connection, or association with Plaintiff's Reveal.

79. Defendant's conduct amounts to deception, trickery, and/or unfair methods and has damaged and jeopardized Plaintiff's business. As a result of such malicious, wanton, and/or fraudulent conduct, Defendant has caused, and unless enjoined by the Court, will continue to cause confusion as to the performance of Signatera in comparison to Plaintiff's Reveal.

80. Plaintiff is entitled to damages for Defendant's unfair competition, an accounting of profits made on sales of Defendant's product, and recovery of Plaintiff's costs of this action. Defendant's actions have been willful and have been undertaken with the purpose of deceiving consumers. Thus, Plaintiff is entitled to an award of punitive damages.

81. As a result of Defendant's conduct, Plaintiff has suffered, and unless such acts and practices are enjoined by this Court, will continue to suffer, damage to its business, reputation, and goodwill for which it is entitled to relief.

V. JURY DEMAND

Plaintiff demands a trial by jury of all issues so triable.

PRAYER FOR RELIEF

WHEREFORE, Plaintiff respectfully prays for the following relief:

A. The Court enter an order temporarily, preliminarily, and permanently enjoining Defendant, its agents, servants, employees, attorneys, successors and assigns, and all others in active concert or participation with them, from directly or indirectly falsely or misleadingly advertising or promoting Signatera in comparison to Reveal;

B. The Court enter an order temporarily, preliminarily, and permanently enjoining Defendant, its agents, servants, employees, attorneys, successors and assigns, and all others in active concert or participation with them, from making or inducing others to make any false, misleading, or deceptive statement of fact, or representation of fact in connection with the promotion, advertisement, display, sale, offering for sale, manufacture, production, circulation or distribution of Signatera in such fashion as to suggest Signatera offers superior clinical performance compared to Reveal; that Reveal lacks appropriate scientific and medical support; or that use of Reveal may be detrimental to patients or could compromise patient care;

C. The Court enter an order requiring that Defendant take corrective action to correct any erroneous impression persons may have derived concerning the nature, characteristics, or qualities of Signatera in comparison to Reveal, including without limitation the placement of corrective advertising;

D. The Court enter an order granting Plaintiff such other relief as the Court may deem appropriate to prevent the trade and public from deriving any erroneous impression concerning the nature, characteristics, qualities, or benefits of Signatera or Reveal;

E. The Court enter an order requiring Defendant to pay Plaintiff damages in an amount sufficient to compensate Plaintiff for injury it has sustained as a consequence of Defendant's unlawful acts, including Plaintiff's actual and consequential damages resulting from Defendant's false and misleading advertisements and marketing and unfair competition pursuant to 15 U.S.C. § 1117(a), CAL. BUS. & PROF. CODE §§ 17200 et. seq. and 17500 et. seq., and

the common law of the State of California;

F. The Court enter an order requiring Defendant to pay Plaintiff damages in the amount of Plaintiff's actual and consequential damages resulting from Defendant's false and misleading advertisements and marketing and unfair competition pursuant to 15 U.S.C. § 1117(a), CAL. BUS. & PROF. CODE §§ 17200 et. seq. and 17500 et. seq., and the common law of the State of California;

G. The Court enter an order requiring Defendant to pay Plaintiff additional damages equal to three times the actual damages awarded Plaintiff pursuant to 15 U.S.C. § 1117(a);

H. The Court enter an order finding that Defendant acted maliciously, wantonly, and/or fraudulently, requiring Defendant to pay Plaintiff punitive damages pursuant to the common law of the State of California;

I. An accounting be directed to determine Defendant's profits resulting from its illegal activities and such profits be paid over to Plaintiff, increased as the Court finds to be just under the circumstances of this case pursuant to 15 U.S.C. § 1117(a);

J. The Court enter an order finding that this case is an exceptional case and requiring Defendant to pay all of Plaintiff's reasonable attorneys' fees, costs and expenses, including those available under 15 U.S.C. § 1117(a), and any other applicable law;

K. The Court enter an order requiring Defendant to pay Plaintiff pre-judgment and post-judgment interest on the damages awarded; and

L. The Court enter an order awarding Plaintiff such other and further relief as the Court deems just and equitable.

Dated: May 27, 2021

NORTON ROSE FULBRIGHT US LLP

By: */s/Saul Perloff*
Saul Perloff

Attorney for Plaintiff
GUARDANT HEALTH, INC.